

LISTING OF THE CLAIMS

1. (Original) A pharmaceutical composition for the treatment of an inflammatory disease comprising:
a water-soluble polymer and an effective amount of an anti-inflammatory therapeutic agent linked to said water-soluble polymer, wherein the water-soluble polymer specifically accumulates in sites of inflammation.
2. (Original) The pharmaceutical composition of claim 1, further comprising a targeting moiety linked to the water-soluble polymer.
3. (Canceled).
4. (Previously Presented) The pharmaceutical composition of claim 1, wherein the water-soluble polymer is selected from the group consisting of a HPMA copolymer, polyethylene glycol, polyglutamic acid, polyaspartic acid, dextran, chitosan, cellulose, starch, gelatin, hyaluronic acid and derivatives thereof.
5. (Previously Presented) The pharmaceutical composition of claim 1, further comprising a bio-assay label linked to the water-soluble polymer.
6. (Previously Presented) he pharmaceutical composition of claim 1, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is cleavable.
7. (Previously Presented) The pharmaceutical composition of claim 1, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is uncleavable.
8. (Original) The pharmaceutical composition of claim 1, wherein the anti-

inflammatory therapeutic agent is a glucocorticoid.

9. (Original) The pharmaceutical composition of claim 2, wherein the targeting moiety directs the composition to bone or cartilage.

10. (Previously Presented) The pharmaceutical composition of claim 2, wherein the targeting moiety is selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicic acid, antibodies and fragments or derivatives thereof.

11. (Previously Presented) The pharmaceutical composition of claim 2, wherein the link between the targeting moiety and the water-soluble polymer is cleavable.

12. (Previously Presented) The pharmaceutical composition of claim 2, wherein the link between the targeting moiety and the water-soluble polymer is uncleavable.

13. (Previously Presented) The pharmaceutical composition of claim 1, wherein the water-soluble polymer comprises N-(2-hydroxypropyl)methacrylamide.

14. (Previously Presented) The pharmaceutical composition of claim 1, wherein the water-soluble polymer comprises one or more monomers selected from the group consisting of, N-(2-hydroxypropyl)methacrylamide, N-isopropyl-acrylamide, acrylamide, N,N-dimethylacrylamide, N-vinylpyrrolidone, vinyl acetate, 2-methacryloxyethyl glucoside, acrylic acid, methacrylic, vinyl phosphonic acid, styrene sulfonic acid, maleic acid, 2-methacryloyloxyethyltrimethylammonium chloride, methacrylamidopropyltrimethylammonium chloride, methacryloylcholine methyl sulfate, N-methylolacrylamide, 2-hydroxy-3-methacryloxypropyltrimethyl ammonium chloride, 2-methacryloyloxyethyltrimethyl ammonium bromide, 2-vinyl-1-methyl-pyridinium bromide,

4-vinyl-1-methylpyridinium bromide, ethyleneimine, (N-acetyl) ethyleneimine, (N-hydroxyethyl)ethyleneimine, allylamine and combinations thereof.

15. (Previously Presented) The pharmaceutical composition of claim 1, wherein the therapeutic agent is selected from the group consisting of proteins, peptides, NSAIDs, DMARDs, glucocorticoids, methotrexate, sulfasalazine, chloriquine, gold, gold salt, copper, copper salt, penicillamine, D-penicillamine, cyclosporine, and mixtures thereof.

16. (Withdrawn) A method for the treatment of an inflammatory disease comprising:
administering the pharmaceutical composition of claim 1 to a subject thought to have an inflammatory disease; and

accumulating the pharmaceutical composition in inflamed tissue of the subject by the affinity of the water-soluble polymer for the inflamed tissue.

17. (Withdrawn) The method according to claim 16, further comprising targeting the water-soluble polymer to a specific tissue.

18. (Withdrawn) The method according to claim 16, wherein the inflammatory disease comprises rheumatoid arthritis.

19. (Canceled).

20. (Withdrawn) The method according to claim 16 further comprising: conducting a biodistribution assay wherein the composition is labeled.

21. (Withdrawn) The method according to claim 16, further comprising cleaving the link between the therapeutic agent and the water-soluble polymer.

22. (Withdrawn) The method according to claim 17, wherein targeting the water-soluble polymer to a specific tissue comprises targeting bone or cartilage.

23. (Withdrawn) The method according to claim 17, wherein targeting the water-soluble polymer to a specific tissue comprises using a targeting moiety selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicic acid, antibodies and fragments or derivatives thereof.

24. (Withdrawn) The method according to claim 17, further comprising cleaving the a link between the targeting moiety and the water-soluble polymer.

25. (Withdrawn) A method of administering an aqueous composition to a subject, said method comprising:

administering the pharmaceutical composition of claim 1 in an aqueous solvent or diluent to a subject thought to have rheumatoid arthritis; and

allowing accumulation and targeting of the pharmaceutical composition in an arthritic joint, thereby improving a treatment of arthritis.

26. (Withdrawn) The method according to claim 25, further comprising reducing a side effect of the therapeutic agent in tissues other than the arthritic joint.

27. (Withdrawn) The method according to claim 25, wherein the therapeutic agent is selected from the group consisting of a NSAIDs, DMARDs, cyclooxygenase-2 inhibitor, a glucocorticoid, a tumor necrosis factor blocker and an interleukin-1 receptor antagonist.

28. (Withdrawn) The method according to claim 25, wherein the water-soluble agent comprises a HEMA copolymer.

29. (Withdrawn) A composition for imaging and evaluating an inflammatory disease comprising:

a water-soluble polymer and an effective amount of a medical imaging agent linked to said water-soluble polymer, wherein the medical imaging agent is used in the

imaging and evaluation of an inflammatory disease.

30. (Withdrawn) The composition of claim 29, further comprising a therapeutic agent linked to said water-soluble polymer.

31. (Withdrawn) The composition of claim 29, wherein the medical imaging agent is selected from the group consisting of at least one of a MRI, PET, CT and γ -scintigraphy agent.

32. (Withdrawn) The composition of claim 29, further comprising a targeting moiety linked to the water-soluble polymer.

33. (Canceled).

34. (Withdrawn) The composition of claim 29, wherein the water-soluble polymer is selected from the group consisting of an HPMA copolymer, polyethylene glycol, polyglutamic acid, polyaspartic acid, dextran, chitosan, cellulose, starch, gelatin, hyaluronic acid and derivatives thereof.

35. (Withdrawn) The composition of claim 29, further comprising a bio-assay label linked to the water-soluble polymer.

36. (Withdrawn) The composition of claim 29, further comprising a spacer between the imaging agent and the water-soluble polymer, wherein the spacer is cleavable.

37. (Withdrawn) The composition of claim 29, further comprising a spacer between the imaging agent and the water-soluble polymer, wherein the spacer is uncleavable.

38. (Withdrawn) The composition of claim 30, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is cleavable.

39. (Withdrawn) The composition of claim 30, further comprising a spacer between the therapeutic agent and the water-soluble polymer, wherein the spacer is uncleavable.

40. (Canceled).

41. (Withdrawn) The composition of claim 32, wherein the targeting moiety directs the composition to bone or cartilage.

42. (Withdrawn) The composition of claim 32, wherein the targeting moiety is selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicyclic acid, antibodies and fragments or derivatives thereof.

43. (Canceled).

44. (Withdrawn) The composition of claim 29, wherein the water-soluble polymer comprises N-(2-hydroxypropyl)methacrylamide.

45. (Withdrawn) The composition of claim 29, wherein the water-soluble polymer comprises one or more monomers selected from the group consisting of N-(2-hydroxypropyl)methacrylamide, N-isopropylacrylamide, acrylamide, N,N-dimethylacrylamide, N-vinylpyrrolidone, vinyl acetate, 2-methacryloxyethyl glucoside, acrylic acid, methacrylic, vinyl phosphonic acid, styrene sulfonic acid, maleic acid, 2-methacryloxyethyltrimethylammonium chloride, methacrylamido-propyltrimethylammonium chloride, methacryloylcholine methyl sulfate, N-methylolacrylamide, 2-hydroxy-3-methacryloxypropyltrimethyl ammonium chloride, 2-methacryloxyethyltrimethylammonium bromide, 2-vinyl-1-methylpyridinium bromide, 4-vinyl-1-methylpyridinium bromide, ethyleneimine, (N-acetyl)ethyl-eneimine, (N-hydroxyethyl)ethyleneimine, allylamine and combinations thereof.

46. (Withdrawn) The composition of claim 30, wherein the therapeutic agent is

selected from the group consisting of proteins, peptides, NSAIDs, glucocorticoids, methotrexate, sulfasalazine, chloriquine, gold, gold salt, copper, copper salt, penicillamine, D-penicillamine, cyclosporine, and mixtures thereof.

47. (Withdrawn) A method for imaging and evaluation of an inflammatory disease in a subject, the method comprising:

administering the composition of claim 29 to the subject; and
imaging an inflammatory disease patient or animal model before and after the administration of the imaging agent with MRI, PET, CT or y-scintigraphy equipment.

48. (Canceled).

49. (Withdrawn) The method according to claim 47, further comprising conducting a biodistribution assay.

50. (Withdrawn) The method according to claim 47, further comprising targeting the water-soluble polymer to a specific tissue.

51. (Withdrawn) The method according to claim 50, wherein targeting of the compound is directed to bone or cartilage.

52. (Withdrawn) The method according to claim 50, wherein targeting the compound to a specific tissue comprises using a targeting moiety selected from the group consisting of bisphosphonates, quaternary ammonium groups, peptides, oligo-Asp, oligo-Glu, aminosalicilic acid, antibodies and fragments or derivatives thereof.

53. (Withdrawn) The method according to claim 50, further comprising cleaving a link between the targeting moiety and the water-soluble polymer.

54. (Withdrawn) The method according to claim 50, wherein imaging an

inflammatory disease patient or animal model enhanced with the compound comprises imaging an arthritic joint.

55. - 56. (Canceled).

57. (Original) The pharmaceutical composition of claim 1, wherein the therapeutic agent comprises a plurality of distinct therapeutic agents.

58. (Previously Presented) The pharmaceutical composition of claim 2, wherein the targeting moiety comprises a plurality of distinct targeting moieties.

59. (Original) The pharmaceutical composition of claim 58, wherein the plurality of distinct targeting moieties target a plurality of tissues.

60. (Original) The pharmaceutical composition of claim 5, wherein the bio-assay label comprises a plurality of distinct bio-assay labels.

61. (Previously Presented) The pharmaceutical composition of claim 6, wherein the spacer comprises a plurality of chemically distinct spacers.

62. (Withdrawn) The composition of claim 31, wherein the imaging agent comprises a plurality of distinct imaging agents.

63. (Withdrawn) The method according to claim 55, wherein the imaging agent comprises at least two imaging agents, wherein each of the two imaging agents is used in a different imaging technique.

64. (Withdrawn) A composition comprising a water-soluble N-(2-hydroxypropyl) methacrylamide copolymer linked to a targeting moiety and to a glucocorticoid via a pH sensitive hydrozone bond.

65. (Withdrawn) The composition of claim 64, wherein the glucocorticoid is dexamethasone.

66. (Withdrawn) The composition of claim 64, wherein the targeting moiety is hydrazine.